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Research Article

Community-Acquired Elizabethkingiameningoseptica with Leucine Aminopeptidase Activity as a Cause of Fatal Sepsis in an adult with Diabetes Mellitus

Marijo S. Roiko[1], Natalia I. Rush[2]*, Patrick DeMoss[3] and Thomas E. Davis[2]

[1]*Department of Pathology and Laboratory Services, Altru Health System, USA*
[2]*Department of Pathology and Laboratory, Indiana University School of Medicine, USA*
[3]*Department of Pediatrics, University of Mississippi Medical Center, USA*

***Corresponding author**

Natalia I. Rush, Department of Pathology and Laboratory Services, Altru Health System, 350 W. 11th Street, Room 4014, Indianapolis, 46260, Indiana, USA, Tel: 317-491-6000; Fax: 317-491-6419; Email: natervin@iupui.edu

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Abstract

Elizabethkingiameningoseptica is an oxidase- and catalase-positive non-fermentative environmental saprophytic Gram-negative rod that can colonize medical devices and equipment due to its ability to form bio films, thus, resisting mechanical and chemical disinfection. This organism is usually associated with multi-drug resistant nosocomial infections. Here, we present a case of community-acquired *E. meningoseptica* in a 73-year-old man with multiple co morbidities, who presented with symptoms, signs, and laboratory data consistent with sepsis and multi-organ dysfunction syndrome. Initial cultures from blood and pleural fluid grew *E. meningoseptica*. Automated antimicrobial susceptibility tests demonstrated resistance to numerous drugs, except for fluoroquinolones. The patient's antibiotic regimen was switched from broad spectrum to levofloxacin with nafcillin on day five of hospital stay. Although the patient cleared *E. meningoseptica* infection, he remained in critical condition and shortly developed nosocomial infections involving the urinary tract with *Candida albicans* and the respiratory tract with *Stenotrophomonas maltophilia* that led to death. In patients who present with severe sepsis caused by non-fermenting Gram-negative bacillus, *E. meningoseptica* should be considered, noting its multi-drug resistance and the potential for a dismal outcome.

ABBREVIATIONS

E. meningoseptica: *Elizabethkingiameningoseptica*; rRNA: Ribosomal Ribonucleic Acid; ED: Emergency Department; PYR: Pyrrolidonyl Aminopeptidase; LAP: Leucine Aminopeptidase; KIA: Kligler Iron Agar

INTRODUCTION

*E.meningoseptica*is an oxidase- and catalase-positive, non-fermentative, non-motile Gram-negative rod that is related to many other clinically significant members of the *Bacteroidetes*, including flavobacteria [1]. The organism has undergone considerable taxonomic revision, and it was previously called *Flavobacterium meningosepticum* (1959), *Chryseobacterium meningosepticum* (1994), and in 2005, it was renamed *E.meningoseptica* based on 16s rRNA phylogenetic analysis [1]. *E. meningoseptica* is ubiquitous in the environment and has been isolated from plants, soil and aquatic habitats [2]. Also, it has been identified to colonize medical devices and equipment, sinks, and even antiseptic solutions, predictably due to its ability to form bio films and resist mechanical and chemical disinfection [3-5]. Associated with its ability to readily colonize environmental surfaces of healthcare environments, infections caused by *E. meningosepticum* are typically contracted nosocomially or as a consequence of invasive proceduare. This organism is not considered to be part of the normal human flora; however, it has been isolated from asymptomatic patients [6,7].

CASE PRESENTATION

A 73-year-old male with poorly controlled type II diabetes presented to ED in septic shock and multi-organ dysfunction syndrome by ambulance. Prior to the paramedic's arrival, the patient complained on a phone of diarrhea and shortness of breath without disclosure of his symptoms' duration. Vital signs and physical examination obtained by the paramedics demonstrated dyspnea, hypotension, tachycardia, and altered mental status. Additional findings gathered in ED included dry mucous membranes and no breath sounds over the right chest. Significant initial laboratory values included serum creatinine of 7.14 mg/dL, pH of 7.27, bicarbonate of 12 mg/dL, albumin of 2.6 g/dL, neutrophilia (15,300 WBC: 88% neutrophils, 1% bands, 7% lymph and 4% monos), hemoglobin of 5.2 mg/dL, and lactate of 6.5 mmol/L. The chest X-ray demonstrated a right pleural effusion. The patient was resuscitated with intravenous fluids, packed red blood cells, and was empirically treated with ceftriaxone and azithromycin. Respiratory and renal failures prompted transfer to the intensive care unit, where the antibiotic regimen was switched to vancomycin and piperacillin/tazobactam. A review of the patient's medical history revealed poorly-controlled diabetes mellitus type II, a stage II decubitus ulcer, obesity, chronic obstructive pulmonary disease, and laryngeal cancer, status post laryngectomy and tracheostomy in 1994.

An initial set of blood culture became positive 13 hours after collection. Gram's stain demonstrated Gram-negative rods that were not identified by Gram-Negative Quick FISH™ (AdvanDx, Inc., Woburn, MA), a rapid method that permits identification of *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* from positive blood cultures. Following overnight incubation of blood culture aliquots on solid media in a CO_2-enriched atmosphere at 35°C, pale yellow colonies grew on 5% sheep blood agar and chocolate agar, but no growth was observed on Mac Conkey agar (Figure 1). The isolate was identified by VITEK®2 (bio Mérieux, Inc., Durham, NC) and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry as *E. meningoseptica* (Bruker Daltonics Inc., Billerica, MA). A summary of all microbiology studies are reported in Table 1. An automated antimicrobial susceptibility testing of this isolate demonstrated resistance to numerous drugs, except for fluoroquinolones (Vitek2, bio Merisux). A report of susceptibility testing is provided in Table 2. *E. meningoseptica* was also isolated from pleural fluid collected on the day after admission and demonstrated an equivalent antimicrobial susceptibility pattern. Cultures of a tracheal aspirate yielded methicillin-susceptible Staphylococcus aureus and a urine culture was negative. Subsequently, the patient's antibiotic regimen was de-escalated to levofloxacin and nafcillin. While blood cultures from day 5 of hospital stay were still positive for *E. meningoseptica*, subsequent blood and pleural fluid cultures were negative. The patient remained in critical condition on vasopressors with signs of anoxic brain injury. On day 9, the patient had urine culture positive for >100,000 colony forming units of *Candida albicans*. On day 11, a sputum culture grew *Stenotrophomonasmaltophilia.* And on day 12, the patient had a blood culture positive for *C. albicans* in the aerobic bottle. The patient succumbed to his illness on hospital day 15.

DISCUSSION

Here we report a case of a community-acquired *E. meningoseptica* leading to fatal sepsis in an adult host. *E. meningoseptica* predominantly causes disease in two patient populations: infants and immune compromised. Infections are most often acquired from healthcare facilities, however, community-acquired meningitis and other disease presentations have been reported [5,7-13]. Although this patient's initial presentation included altered mental status, which could have been related to meningitis, we have no evidence to support this. Upon admission, a cerebrospinal fluid specimen was not collected for laboratory analysis and, after the patient's death; the family members declined an autopsy, which precluded acquisition of post-mortem evidence of meningitis.

Reported co morbidities in patients infected with *E. meningoseptica* include an immune compromised state, chronic debilitating diseases, including diabetes, malignancy, congestive heart failure, and invasive medical device placement, such as a central line or mechanical ventilator [5,8,9,14]. In this case, the patient had poorly-controlled type II diabetes with a tracheostomy and the stage II decubitus ulcer. However, it is not clear if the compromised barriers were a conduit for his infection, as the patient did not present with an active wound infection and

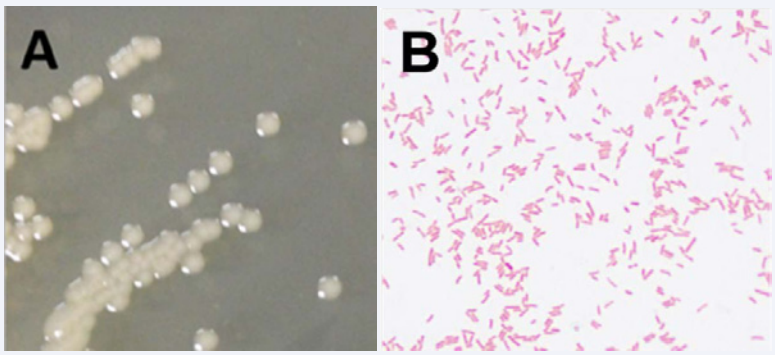

Figure 1 A. Overnight growth on brain heart infusion agar illustrates pale yellow colonies of *E. meningoseptica.*
B. Gram stain from overnight growth on sheep blood agar demonstrates straight and slightly- curved Gram-negative rods measuring 1-2 x 0.5 µm (1000x original magnification).

Table 1: Summary of laboratory studies on E. meningoseptica isolate.

Test	Result
Culture characteristics	
Sheep blood agar	Non-hemolytic
Mac Conkey agar	No growth*
Pigment	Pale yellow
Growth at 42°C	No growth
Biochemical properties	
Oxidase	+
Catalase	+
Indole	+
DNase	+
Gelatinase	+
Pyrrolidonyl aminopeptidase	+
Leucine aminopeptidase	+**
Esculin hydrolysis	+
Urease	-
Motility	-
Colistin	Resistant
Kligler Iron Agar	K/K
Carbohydrate substrate	Oxidation/Fermentation
Glucose	+/-
Mannitol	+/-
Xylose	-/-
Lactose	-/-
Sucrose	+/-
Maltose	+/-
Abbreviations: K/K = alkaline/alkaline; *Not characteristic finding; **Not previously reported	

Table 2: Antimicrobial susceptibility.

Antibiotic	MIC	Interpretation
Amikacin	>=64	R
Ampicillin/Sulbactam	>=32	R
Cefepime	>=64	R
Ceftazidime	>=64	R
Ceftriaxone	>=64	R
Ciprofloxacin	1	S
Gentamicin	>=16	R
Levofloxacin	0.5	S
Meropenem	>=16	R
Piperacillin/Tazobactam	>=128	R
Tobramycin	>=16	R
Trimethoprim/ Sulfamethoxazole	>=80	R
Abbreviations: MIC = Minimum Inhibitory Concentration		

there was no evidence for respiratory colonization, as a tracheal aspirate did not grow *E. meningoseptica*.

*E. meningoseptica*is infrequently isolated in the clinical microbiology laboratory and may be challenging to identify. Key biochemical characteristics for this non-fermentative Gram-negative rod are positive oxidase, catalase, and indole reactions. Although the majority of *E. meningoseptica* strains grow on Mac Conkey agar, this isolate failed to do so, despite prolonged incubation. In addition to positivity for PYR and esculin hydrolysis by the Strep quick method (Hardy Diagnostics, Santa Maria, CA), the isolate was strongly positive for LAP, a result not previously reported.

Isolates of *E. meningoseptica* are frequently multi-drug resistant [14,15]. An antibiotic susceptibility testing for this organism should be performed by broth micro-dilution as disk diffusion methods may be erroneous [2,20]. Resistance to cephalosporins and carbapenems has been reported to be associated with serine and metallo-beta-lactamases, which may be chromosomally encoded [16-19]. *E. meningoseptica*can also acquire resistance to antibiotics, including resistance to erythromycin, rifampin, and sulfonamides [21-28]. In our case, the isolate was susceptible to fluoroquinolones.

No standard treatment guidelines have been developed for *E. meningoseptica* and the organism may not respond to antibiotics typically used for Gram-negative infections, such as beta-lactams, including carbapenems, and aminoglycosides [14]. Unusually, antibiotics for Gram-positive infections like fluoroquinolones, trimethoprim-sulfamethoxazole, vancomycin, and rifampin are effective [2,8,9,14,15,29,30]. Suggested antibiotic regimens include trimethoprim-sulfamethoxazole and fluoroquinolones, minocycline, or rifampin plus piperacillin [2,8,9,15,30]

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